DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health

Memorandum

Date March 19, 1986

From Chief, Laboratory of Tumor Cell Biology, DTP, DCT, NCI

Subject CEM line for testing

To Dr. Lowell Harmison, OASH

I have heard that there has been talk that the Genetics System test using LAV in CEM cell line has some advantages. I also hear that the "English" (Burroughs Wellcome) test is making an attempt to sell in the U.S. again using the CEM cell line.

I want to remind our negotiating officials that the CEM cell line was first used by our lab as a permissive line. The patent covering the methodology for growing HTLV-III includes the H9, CEM, Molt-3, and HUT 78 cell lines. HTLV-III production from CEM/HLTV-III appears to be about as good quantitatively as H9, but may be less stable. Therefore, 2 1/2 years ago we selected H9 over CEM. Reinfection of CEM cells may sometimes be necessary to carry the virus and this can be a long-term serious disadvantage. There is also overall much less experience with CEM and consequently a larger unknown potential for difficulty in production. For example, it is not known whether HTLV-III is integrated in the CEM line. Just as H9 is a clone of the HT line, clones of the CEM line may have different characteristics with regard to growth, virus production, stability, variation of virus in culture, and relative antigen expression. The consensus is that CEM offers no intrinsic advantage in virus production and may have yet to be discovered disadvantages. Therefore, I would strongly urge our FDA officials to get input from very experienced people (like us) before making public quality pronouncements.

Also, the nature of "false postive" Elisa tests must be considered in discussing claims of specificity. First, obviously, the standard by which the Elisa is judged must be the same to make any valid comparisons between groups. The claim that virus grown in CEM has no HLA-DR antigen and therefore no false positives (100% specificity) is premature. First, most false positive Elisa tests are not due to antibodies directed to HLA-DR antigens in the virus preparation. The procedures used to prepare some test kits may, in fact, eliminate positive results due to HLA. It is entirely likely that false postive samples will be scored differently in different kits although the overall rates are comparable. Second, we must realistically expect some false postive Elisa results in sera no matter which test is used. The use of CEM cells does not avoid the necessity to compare all tests to a uniform standard for sensitivity and specficity and evaluation of difficult sera. I am certain that in the long run it is much wiser to have a modestly higher false positive screening result than to have a higher false negative result; we realize that there must be a balance.

The current manufacturers have had the most experience evaluating the strengths and weaknesses of their respective assays in the field and might be able to comment on the relative merits of and potential pitfalls in introducing the CEM line for large scale virus production for screening. However, in the future I would strongly urge our officials, FDA or otherwise, to get input from experts in this field before making public or semi-public pronouncements on the value of the CEM line.

Finally, does anyone know why this pending patent has not been issued? Clearly, no group could grow the virus in a cell line until our success. We established the only patent on this for the U.S. Government and as noted above it includes CEM which we first successfully infected in 1983.

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